

Press Release

Diabetes drug modulates cholesterol levels

Neuherberg, July 6, 2015. **Besides affecting the blood sugar levels, the substance Metformin, also has an impact on blood fat levels. This was elucidated by an interdisciplinary team of the German Center for Diabetes Research (DZD) headed by Dr. Rui Wang-Sattler of the Helmholtz Zentrum München. Especially the harmful LDL cholesterol can be reduced. The results have recently been published in the journal 'Diabetes Care'.**

The DZD-researchers at Helmholtz Zentrum München and German Diabetes Center Düsseldorf analyzed more than 1.800 blood samples of participants, who joined the German large-scale study KORA*. Using a comprehensive approach, the scientists investigated metabolic products (metabolites) as well as genetics of these participants. They found that the administration of Metformin** in patients suffering from Type 2 Diabetes led to a change in metabolite levels. According to the authors, this was associated with a significantly decreased level of LDL cholesterol***, which is under strong suspicion to promote cardiovascular diseases by causing atherosclerosis.

Metformin affects blood fat levels via AMPK signaling pathway

Together with colleagues in the Netherlands, the scientists aligned the metabolite concentrations with the genetic information, thereby identifying metabolites and genes involved in the respective pathways. "We speculate that Metformin intake affects the levels of LDL cholesterol via AMPK****, leading to a down-regulation of the genes FADS1 and 2. This is also supported by the fact that three lipid metabolites, which are dependent on FADS, are decreased. Presumably, this is the mechanism how the production of LDL cholesterol is repressed by Metformin.", reports Dr. Rui Wang-Sattler, head of the group 'Metabolism' in the Research Unit of Molecular Epidemiology at the Institute of Epidemiology II of the Helmholtz Zentrum München.

„Our study suggests that Metformin might indeed have an additional beneficial effect with regards to cardiovascular diseases among the Diabetes patients“, says first author Dr. Tao Xu. Moreover, the Helmholtz scientists aim to elucidate how Metformin, which is used in the clinic for over 50 years, works on the molecular level. "Until now the exact mechanism is unclear. Thus, we want to continue our contribution to its decryption", co-first author Dr. Stefan Brandmaier adds.

Further information

Background

* For more than 20 years, the Cooperative Health Research in the Region of Augsburg (KORA) has been examining the health of thousands of citizens in Augsburg and environs. The aim of the project is to increase understanding of the impact of environmental factors, behaviour and genes on human health. The KORA studies focus on matters relating to the development and progression of chronic diseases, in particular myocardial infarction and diabetes mellitus. To that end, research is conducted into risk factors arising from lifestyle factors (including smoking, diet and exercise), environmental factors (including air pollution and noise) and genetics. Questions relating to the use and cost of health services are examined from the point of view of health services research.

** Metformin is the oldest and most frequently used oral anti-Diabetes drug. Clinical studies have already shown that it inhibits gluconeogenesis in the liver. However, the mode of action is not understood in detail so far.

*** Low Density Lipoprotein (LDL) is a blood fat transporting protein.

**** The AMP activated protein kinase (AMPK) is an enzyme. It is regulated by the AMP and ATP levels of the cell and is therefore able to determine the energy status of the cell. In case, the energy status is low, AMPK stops energy consuming processes like the synthesis of cholesterol or fatty acids.

Original publication:

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Link to the original publication:

<http://care.diabetesjournals.org/content/early/2015/07/27/dc15-0658.abstract>

As German Research Center for Environmental Health, **Helmholtz Zentrum München** pursues the goal of developing personalized medical approaches for the prevention and therapy of major common diseases such as diabetes mellitus and lung diseases. To achieve this, it investigates the interaction of genetics, environmental factors and lifestyle. The Helmholtz Zentrum München has about 2,300 staff members and is headquartered in Neuherberg in the north of Munich. Helmholtz Zentrum München is a member of the Helmholtz Association, a community of 18 scientific-technical and medical-biological research centers with a total of about 37,000 staff members.

The **Research Unit of Molecular Epidemiology** (AME) analyses population-based cohorts and case studies for specific diseases, using genomics, epigenomics, transcriptomics, proteomics, metabolomics and functional analyses. The aim of this research unit is to decipher the molecular mechanisms of complex diseases like Type 2 Diabetes or Obesity. The unit administers the biological specimen repository of the Department of Epidemiology and stores the samples for national and international projects.

The **Institute of Epidemiology II** (EPI II) focuses on the assessment of environmental and lifestyle risk factors which jointly affect major chronic diseases such as diabetes, heart disease and mental health. Research builds on the unique resources of the KORA cohort, the KORA myocardial infarction registry, and the KORA aerosol measurement station. Aging-related phenotypes have been added to the KORA research portfolio within the frame of the Research Consortium KORA-Age. The institute's contributions are specifically relevant for the population as modifiable personal risk factors are being researched that could be influenced by the individual or by improving legislation for the protection of public health.

The **German Center for Diabetes Research** (DZD) is a national association that brings together experts in the field of diabetes research and combines basic research, translational research, epidemiology and clinical applications. The aim is to develop novel strategies for personalized prevention and treatment of diabetes. Members are Helmholtz Zentrum München – German Research Center for Environmental Health, the German Diabetes Center in Düsseldorf, the German Institute of Human Nutrition in Potsdam-Rehbrücke, the Paul Langerhans Institute Dresden of the Helmholtz Zentrum München at the University Medical Center Carl Gustav Carus of the TU Dresden and the Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Zentrum München at the Eberhard-Karls-University of Tuebingen together with associated partners at the Universities in Heidelberg, Cologne, Leipzig, Lübeck and Munich.

The **Institute for Structural Biology** (STB) investigates the spatial structures of biological macromolecules, their molecular interactions and dynamics using integrated structural biology by combining X-ray crystallography, NMR-spectroscopy and other methods. Researchers at STB also develop NMR spectroscopy methods for these studies. The goal is to unravel the structural and molecular mechanisms underlying biological function and their impairment in disease. The structural information is used for the rational design and development of small molecular inhibitors in combination with chemical biology approaches.

The **Institute of Human Genetics** (IHG) at the Helmholtz Zentrum München and the Technical University of Munich: The Institute is concerned with identifying genes associated with disease and characterizing their

functions. The main aim of the research projects is to develop disease-related genetic variation in humans and mice as well as to develop chromosome analysis techniques and new methods for dealing with specific issues in the sphere of pre- and post-natal diagnostics and tumor cytogenetics.

The aim of the **Institute of Bioinformatics and Systems Biology (IBIS)** is to analyze and interpret biological data to capture information on the etiology and progression of human diseases. The focus is on qualitative and quantitative modeling, on the interconnection of metabolic profiles with genetic variance, on the systematic interpretation of high throughput data and on the systems biology of small molecules. Moreover, IBIS is in charge of the administration of the Munich Information Center for Protein Sequences (MIPS) containing genetic datasets or microbial and plant genomes.

The **Institute of Health Economics and Health Care Management (IGM)** examines approaches to improving the effectiveness and efficiency of health care. The health care system faces the challenge of delivering high-quality, economically viable medical services to meet the needs of the population. Rapid advances in medical technology and fast-changing demographics further aggravate this problem. A firmly based evaluation of the effectiveness and efficiency of health care structures and processes is therefore an essential prerequisite for a rational health care policy.

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